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(71)(72) Applicant and Inventor: ØSTERGAARD, Leif [DK/DK]; Jacob Knudsens Vej 5, DK–8230 Aabyhøj (DK).

(74) Agent: PLOUGMANN, VINGTOFT & PARTNERS A/S; Sankt Annæ Plads 11, P.O. Box 3007, DK–1021 Copenhagen K (DK).

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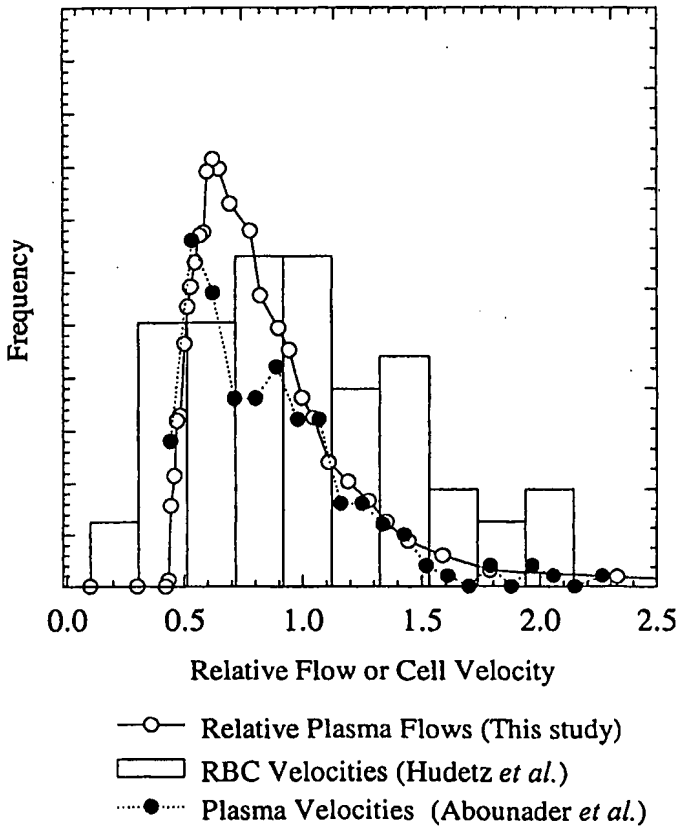
(54) Title: METHOD FOR DETERMINING HAEMODYNAMIC INDICES BY USE OF TOMOGRAPHIC DATA

(57) Abstract

Haemodynamic indices of an organ or a part of tissue are determined from a time series of tomographic data obtained by means of Magnetic Resonance Imaging. Maps of indices are produced, being significant of the dynamics of the capillary tissue flow acquired during rapid bolus injection of a tracer that stays mainly intravascular. The method may be used for evaluating the efficacy of a drug on an organ, or for obtaining information of the likelihood of recovery of an organ or part of tissue upon or during a period of insufficient vascular supply or during the progression of a chronic disease. The method may be used for discriminating between relevant therapy of an organ.



Instead, image elements containing partly tissue, partly blood vessels, must be used in order to characterise the mere shape of the arterial input curve to the tissue. In such cases, absolute values of flow and volume cannot be found, and therefore a normalisation routine allowing (a) comparison of serial measurements in a single subject, (b) comparison among subjects and (c) absolute quantification the case of susceptibility MRI of the brain is described below.

OVERVIEW

The techniques consist of the following steps:

A. Conversion of tomographic images into images representing concentrations of contrast agent as a function of time.

B. Identification of relative or absolute (i.e. in units identical to those of the tomographic images after the above mentioned conversion) arterial tracer concentrations from the image data.

C. In the case of *relative* arterial tracer concentrations, normalisation of the arterial input area to the injected dose of contrast agent per kg body weight.

D. Optional correction of tissue tracer curves for delays.

E. Determination of

   (i) absolute or relative tissue blood flow

   (ii) tissue impulse response function

by deconvolution of tissue concentration time curves by the arterial tracer concentration in each image element.

F. Determination of tissue blood volume by determining the area under the tissue first-pass concentration curve.

G. Determination of tissue mean transit time by the tissue blood volume – blood flow ratio.

H. In the case of MR susceptibility contrast imaging using Gd-chelates in brain tissue, conversion to absolute blood flow and blood volume by a pre-determined constant.

I. Determination of the distribution of flow or transit times in each image element from the residue function (normalised impulse response function) determined in E.

J. Comparison of distributions of relative flows to a predetermined distribution found for a normal organ; here brain.

K. Quantification of the distribution of flows in terms of the extraction fraction of a given solute with specified capillary permeability, in cases where imaging is performed with MR imaging with microvascular weighting, or microvascular volume can otherwise be inferred from total blood volumes.

1. Conversion of tomographic data into tracer concentration images

The method and associated software handles various modalities, depending on whether tracer injection changes signal intensity from baseline in a linear or logarithmic fashion upon tracer arrival. With a specified option, acquired tomographic images during tracer bolus injection are converted into concentrations as a function of time, with measurement time points spaced equally in time.

1.1. In the case of MR images, weighted towards the transverse relaxation times (T_2 or T_2^*), (typically acquired in brain), the tissue concentration as a function of time, $C_t(t)$, is typically obtained by the formula

$$C_t(t) = -k \cdot \log\left(\frac{S(t)}{S(t_o)}\right) / TE \qquad \text{Eq. 1}$$

where $S(t_0)$ is the signal intensity before contrast injection (formed as the average of signal intensities up to tracer arrival), S(t) is the signal intensity at time t, and TE is the echo time used in the sequence. Here, *k* is a constant characteristic of the tissue and contrast agent.

1.2. In the case of MR images weighted towards the longitudinal relaxation time (T_1) images (typically acquired for intravascular tracers in the heart), concentrations are assessed directly by the change in longitudinal relaxation rate, ΔR_1, as derived from signal intensity changes

$$C_t(t) = \Re \cdot \Delta R_1 \qquad \text{Eq. 2}$$

where $\Re$ is the relaxivity of the applied contrast agent.

1.3. In the case of Computed Tomography (CT) images, concentrations are assessed by the change in image intensity, measured in Hounsfield units, ΔH

$$C_t(t) = \kappa \cdot \Delta H \qquad \text{Eq. 3}$$

where κ is the characteristic X-ray absorption of the contrast agent.

2. Identification of Arterial Vessels

For identification of arterial vessels in the image, the algorithm provides the choice of first producing an image that guides this process (2.a.), or proceeding directly to calculation of tissue flow (2.b.)

2.a. If so specified by an option, the concentration time curve of each image element is fitted to a gamma variate function by nonlinear least-squared regression (by means of a fletcher-algorithm) over the time interval until visible tracer re-circulation occurs (the re-circulation is specified by the user, determining

(a) Tracer arrival time
(b) Area under first pass (this quantity is proportional to the local blood volume).

These two quantities are stored as floating point binary image file, allowing visualisation as an image where each image pixel corresponds to quantities (a) and (b), respectively. An artery is then visually identified in these images by

(a) Anatomical location.
(b) Early tracer arrival relative to the arrival in tissue.
(c) Large area under first pass (corresponding to a large blood volume and thereby a large portion of the vascular volume being contained in a voxel).

2.b. By observing images of tracer concentration as a function of time in a tool that allows visualisation of the time-course of single pixels, arterial levels can be identified.

Upon identification of the arterial input function, the corresponding signal intensity time curve is fed to the program below in the form of an ASCII file.

3. Normalisation of Arterial Input to Allow Comparison of Serial Measurements